

EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Specification:****Please amend the paragraph on page 3, lines 26-38, as follows:**

In one embodiment, a kinase encoding a nucleic acid molecule of the invention is at 75%, 77%, 80%, 82%, 85%, 87%, 90%, 92%, 95%, 97%, 98%, 99% or greater homology to a nucleotide sequence (e.g., to the entire length of the nucleotide sequence) including SEQ ID NO:1 or a complement thereof. [] In a preferred embodiment, the isolated nucleic acid molecule includes the nucleotide sequence shown SEQ ID NO:1 or a coding region of SEQ ID NO:1, or a complement thereof. In another embodiment, the nucleic acid molecule includes the 5' UTR and the coding region of SEQ ID NO:1. In yet another embodiment, the nucleic acid molecule includes the coding region of [SEQ ID NO:3] SEQ ID NO:1 and the 3' UTR of SEQ ID NO:1. In another preferred embodiment, the nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1 or the coding region of SEQ ID NO:1. In another preferred embodiment, the nucleic acid molecule comprises a fragment of at least 4400 nucleotides of the nucleotide sequence of SEQ ID NO:1 or the coding region of SEQ ID NO:1, or a complement thereof.

Please amend the paragraph on page 7, lines 3-8, as follows:

Figures [7 a-n] 7 a-a3 comprise various regions of SEQ ID NO:2, as well as comparison sequences, [(SEQ ID NOS: 7-32)](SEQ ID NOS: 8-33), data generated to show PFAM cites, hydrophobicity/ hydrophilicity, and cysteine residues of the amino acid sequence of SEQ ID NO:2, as well as PSORT prediction of protein localization, signal peptide predictions, transmembrane segments predicted by MEMSAT, Prosite pattern matches, protein family/domain matches and ProDom matches of the amino acid sequence of SEQ ID NO:2.

Please amend the paragraph on page 7, lines 25-29, as follows:

Figures 1 a-k depict[s] the cDNA sequence and predicted amino acid sequence of human kinase. The nucleotide sequence corresponds to the 5525 nucleic acids of SEQ ID NO:1 which include nucleic acids 1-4950 of the coding region (SEQ ID NO:3), the 5' UTR of 62 nucleic acids, and the 3' UTR of 513 nucleic acids. The amino acid sequence corresponds to amino acids 1 to 1650 of SEQ ID NO:2.

Please amend the paragraph on page 8, lines 30-31, as follows:

Figures [2 a-c] 2 a-i show a multiple sequence alignment of the amino acid sequence of SEQ ID NO:2 in comparison with known mouse [(SEQ ID NO:4)](SEQ ID NO:5) and human [(SEQ ID NO:3)](SEQ ID NO:4) kinase.

Please amend the paragraph on page 10, lines 2-18, as follows:

In one embodiment, the isolated proteins of the present invention, preferably 14790 proteins, are identified based on the presence of at least one "Ser/Thr kinase site" and at least one "ATP-binding region." As used herein, the term "Ser/Thr kinase site" includes an amino acid sequence of about 200-400 amino acid residues in length, preferably 200-300 amino acid residues in length, and more preferably 250-300 amino acid residues in length, which is conserved in kinases which phosphorylate serine and threonine residues and found in the catalytic domain of Ser/Thr kinases. Preferably, the Ser/Thr kinase site includes the following amino acid consensus sequence X₉-g-X-G-X₄-V-X₁₂-K-X-(10-19)-E-X₆₆-h-X₈-h-r-D-X-K-X₂-N-X₁₇-K-X₂-D-f-g-X₂₁-p-X₁₃-w-X₃-g-X₅₅-R-X₁₄-h-X₃ [(SEQ ID NO:5)](SEQ ID NO:6) (where invariant residues are indicated by upper case letters and nearly invariant residues are indicated by lower case letters). The nearly invariant residues are usually found in most Ser/Thr

kinase sites, but can be replaced by other amino acids which, preferably, have similar characteristics. For example, a nearly invariant hydrophobic amino acid in the above amino acid consensus sequence would most likely be replaced by another hydrophobic amino acid. Ser/Thr kinase domains are described in, for example, Levin D.E. *et al.* (1990) Proc. Natl. Acad. Sci. USA 87:8272-76, the contents of which are incorporated herein by reference.

Please amend the paragraph on page 10, lines 19-26, as follows:

As used herein, the term "ATP-binding region" includes an amino acid sequence of about 5-40, preferably 5-25, and more preferably 5-15 amino acid residues in length, present in enzymes which activate their substrates by phosphorylation, and involved in binding adenosine triphosphate (ATP). ATP-binding regions preferably include the following amino acid consensus sequence: G-X-G-X-X-G-X(15-23)-K [(SEQ ID NO:6)](SEQ ID NO:7). ATP-binding regions are described in, for example, Samuel K.P. *et al.* (1987) FEBS Let. 218(1): 81-86, the contents of which are incorporated herein by reference. Amino acid residues 596-604 of kinase comprise an ATP-binding region.

Please amend the paragraph on page 11, lines 26-34, as follows:

The nucleotide sequence of the isolated human kinase cDNA and the predicted amino acid sequence of the human 14790 polypeptide are shown in Figure 1 and in SEQ ID NOs:1 and 2, respectively. [A plasmid containing the nucleotide sequence encoding human kinase was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made

merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.]

Please amend the paragraph on page 15, line 20 through page 16, line 4, as follows:

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15, 20, 25, 30 or more nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, or the coding region thereof. In other embodiment, the nucleic acid is at least 30, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, or 4500 nucleotides in length. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 30%, 40%, 50%, or 60% homologous to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85% or 90% homologous to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C. A more preferred example of stringent hybridization conditions is hybridization in 0.5M sodium [phosphate] phosphate, 7% SDS at 65°C , followed by one or more washes in 0.2 X SSC at 65°C. Preferably, an isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, or the coding region thereof, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid

molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

Please amend the paragraph on page 62, line 35 through page 63, line 6, as follows:

The sequences of the positive clones were determined and found to contain open reading frames. The nucleotide sequence encoding the human 14790 protein is shown in Figure 1 and is set forth as SEQ ID NO:1. The protein encoded by this nucleic acid comprises about 1650 amino acids and has the amino acid sequence shown in Figure 1 and set forth as SEQ ID NO:2. The coding region (open reading frame) of SEQ ID NO:1 is shown in Figure 1 as the portion of the nucleotide sequence corresponding to the amino acid sequence of SEQ ID NO:2. [The clone comprising the entire coding region of human kinase was deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, 1998, and assigned Accession No. _____.]

Please amend the paragraph on page 63, line 18-25, as follows:

14790 mRNA was found to be expressed in human skeletal muscle, brain and liver. TaqMan RT-PCR analysis revealed that 14790 mRNA was found to be upregulated in liver cells which were infected with HBV. Moreover, mRNA expression of 14790 was found to be restricted to hepatocytes of HBV infected livers as seen b[u]y in situ hybridization. 14790 mRNA was also found to be upregulated in HepG2.2.15 cells (HBV positive) compared to HepG2 parent cells (HBV negative). When HepG2.2.15 cells were treated with anti-HBV drug treatment, the upregulation of 14790 mRNA was eliminated. Thus indicating that a modulator of 14790 activity or mRNA may be used to treat infection by HBV.

In the Claims:

1. (Amended) An isolated nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:1; and

(b) a nucleic acid molecule comprising [the coding region] nucleotides 63 to 4991 of the nucleotide sequence set forth in SEQ ID NO:1.

3. (Amended) An isolated nucleic acid molecule [selected from the group consisting of:

(a) a nucleic acid molecule] comprising [the nucleotide sequence contained in the plasmid deposited with ATCC® as Accession Number _____] the nucleotide sequence set forth in SEQ ID NO:1.

4. (Amended) An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide having kinase activity comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1 or [the coding region] nucleotides 63 to 4991 of SEQ ID NO:1 in 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes in 0.2 X SSC at 65°C [under stringent conditions].

5. (Amended) An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule comprising a nucleotide sequence which is at least [60] 85% homologous to the nucleotide sequence of SEQ ID NO:1 or at least 90% homologous to [the coding region] nucleotides 63 to 4991 of SEQ ID NO:1;

b) a nucleic acid molecule comprising a fragment of at least [200] 3500 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or [the coding region] nucleotides 63 to 4991 of SEQ ID NO:1, or a complement thereof;

c) a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least about [60] 95% homologous to the amino acid sequence of SEQ ID NO:2; and

d) a nucleic acid molecule comprising a fragment of at least 3500 nucleotides which encodes [a fragment of] a polypeptide comprising a fragment of the amino acid sequence of SEQ ID NO:2[, wherein the fragment comprises at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2];

wherein the nucleic acid molecule encodes a polypeptide having kinase activity.

Please delete claim 6 without prejudice or disclaimer.

7. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence which is completely complementary to the nucleotide sequence of the nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5.

12. (Amended) A method of producing a polypeptide comprising culturing a host cell transfected with the vector of claim 9 in an appropriate culture medium to, thereby, produce the polypeptide expressed by the nucleic acid molecule.

22. (Amended) A kit comprising a nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5 to a compound [a compound] which selectively hybridizes in 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes in 0.2 X SSC at 65°C, to a compound [a nucleic acid molecule of any one of claims 1, 2, 3, 4, or 5] and instructions for use.

Please delete claims 27, 29-30 without prejudice or disclaimer.

sd-80276